Effects of Sacubitril/Valsartan on N-Terminal Pro-B-Type Natriuretic Peptide in Heart Failure with Preserved Ejection Fraction

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Speaker's Disclosures

Jonathan Cunningham has no relationships with industry to disclose.

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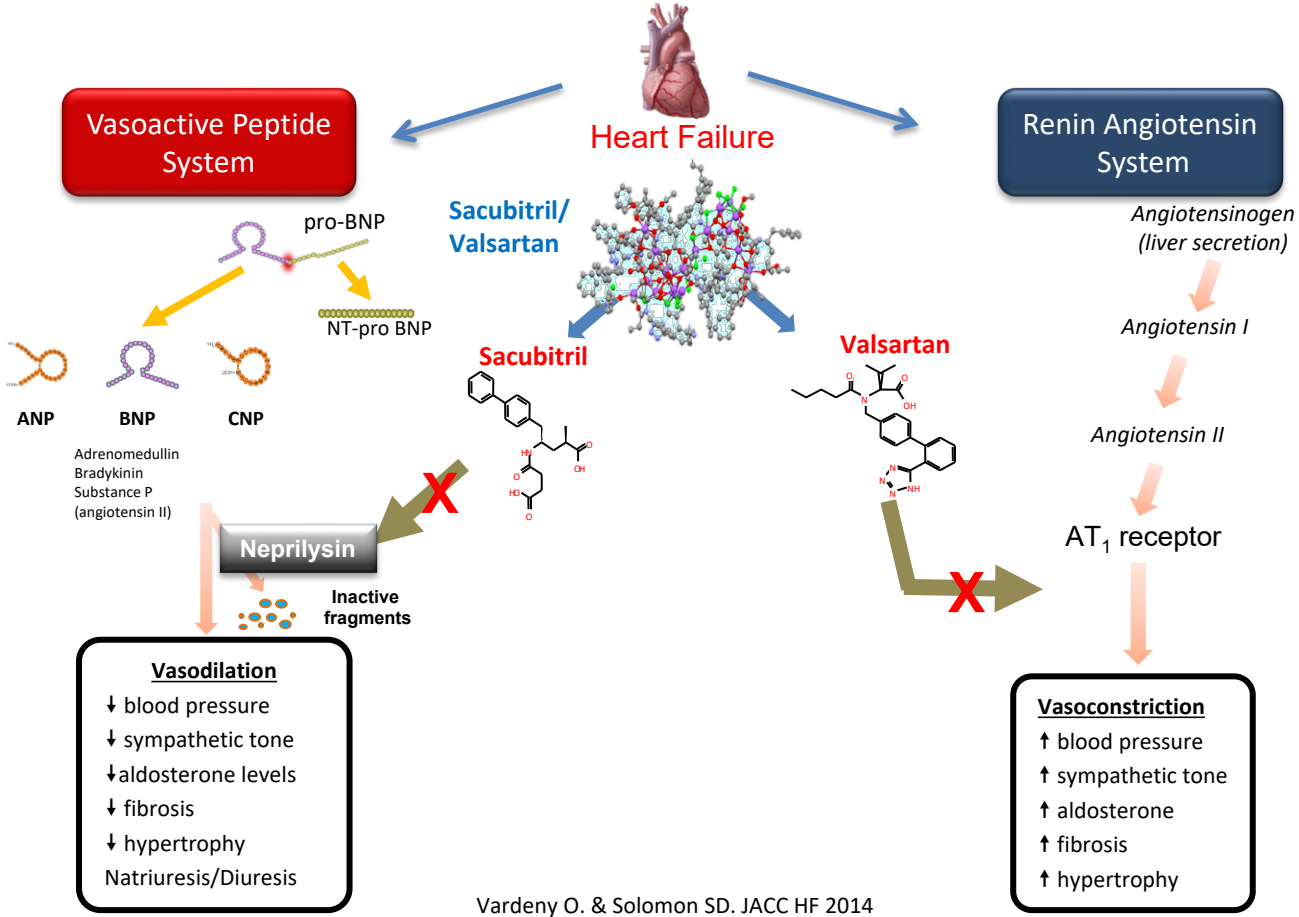
Sacubitril/Valsartan –Angiotensin Receptor Neprilysin Inhibitor – Simultaneously Inhibits NEP and the RAS



Vardeny O. & Solomon SD. JACC HF 2014

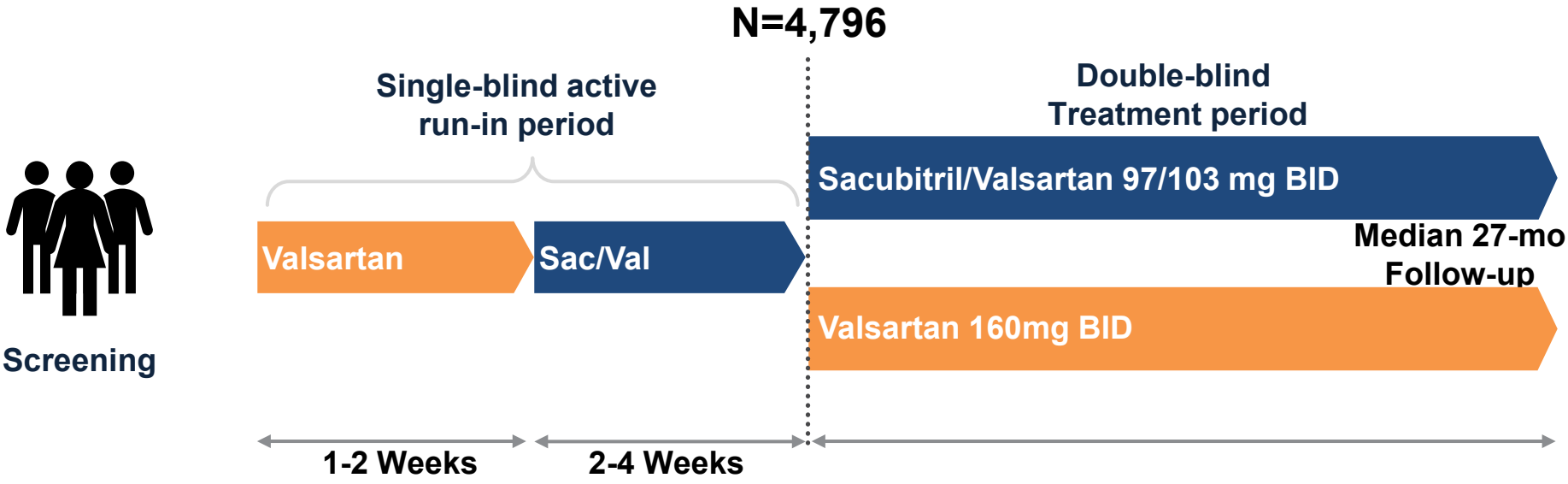
PARAGON-HF Study Design

Key Eligibility Criteria

- Age ≥50 years
- EF ≥45%
- Elevated Natriuretic Peptides
- Structural Heart Disease

Minimum NT-proBNP for Inclusion

- >200 pg/ml with HF hospitalization
- >300 pg/ml without hospitalization
- 3-fold increase in AF



PARAGON-HF Study Design

n=4,757
Screening

Screening

N=4,796

Single-blind active run-in period

Double-blind Treatment period

Valsartan

Sac/Val

Sacubitril/Valsartan 97/103 mg BID

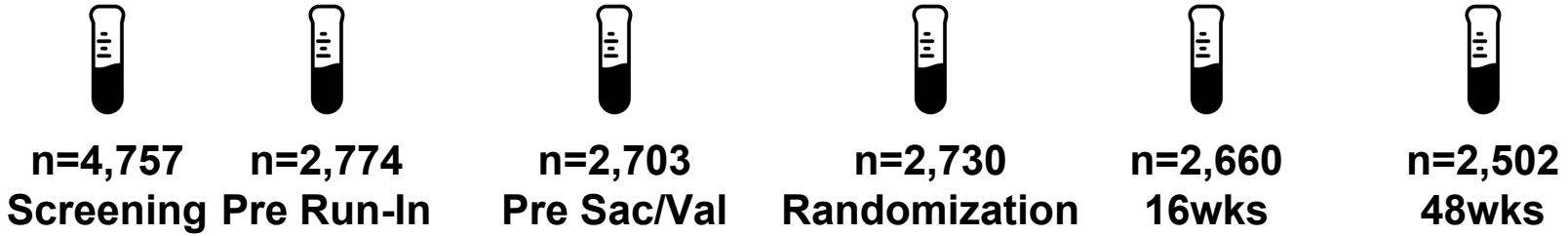
Valsartan 160mg BID

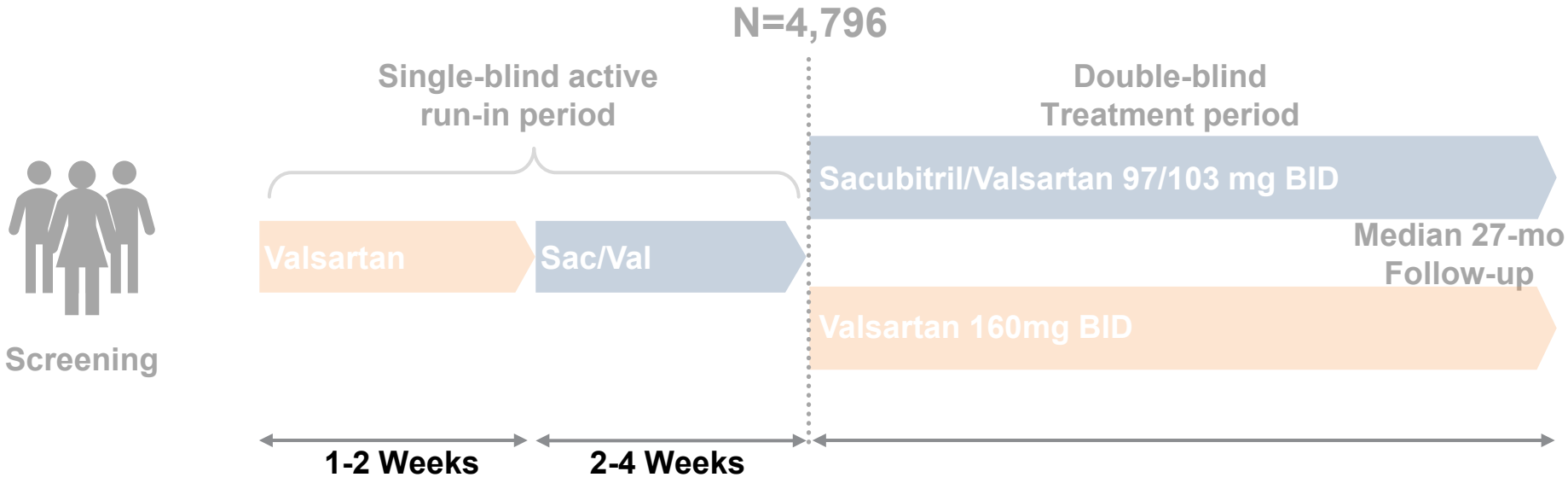
Median 27-mo Follow-up

1-2 Weeks

2-4 Weeks

PARAGON-HF Study Design





Objective

To investigate the relationship between NT-proBNP and outcomes in patients with HFpEF, and the effect of sacubitril/valsartan on NT-proBNP

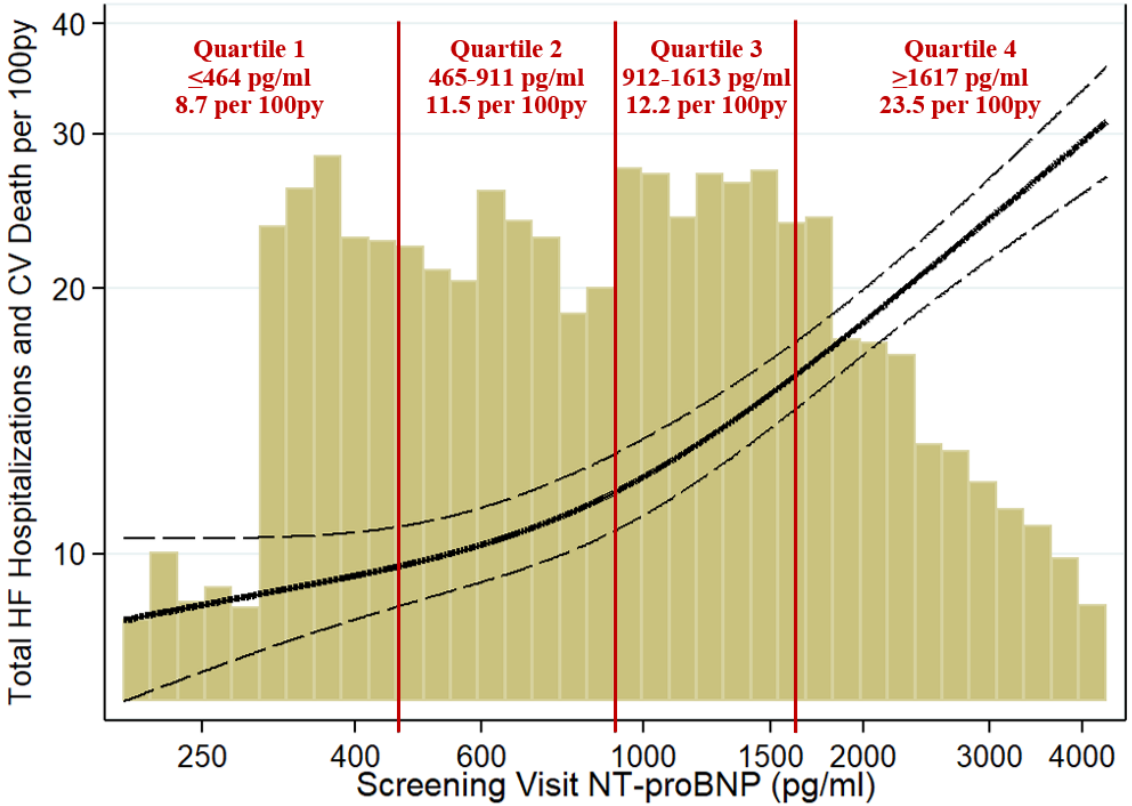
Baseline Characteristics in Each NT-proBNP Quartile

	Quartile 1 n=1190	Quartile 2 n=1189	Quartile 3 n=1189	Quartile 4 n=1190	P-value
NT-proBNP (pg/ml)	<464	465-911	912-1613	1617-31,522	
Age (years)	70.8 ± 8.4	72.6 ± 8.4	73.3 ± 8.2	74.4 ± 8.3	<0.001
Women	56%	53%	47%	51%	0.002
Race					0.85
White	81%	80%	84%	81%	
Asian	12%	13%	12%	14%	
Black	2%	3%	2%	2%	
Other	5%	4%	3%	4%	
Diabetes	46%	43%	42%	42%	0.06
Prior HF Hosp	53%	53%	41%	53%	0.66
Atrial Fibrillation	1%	10%	55%	63%	<0.001

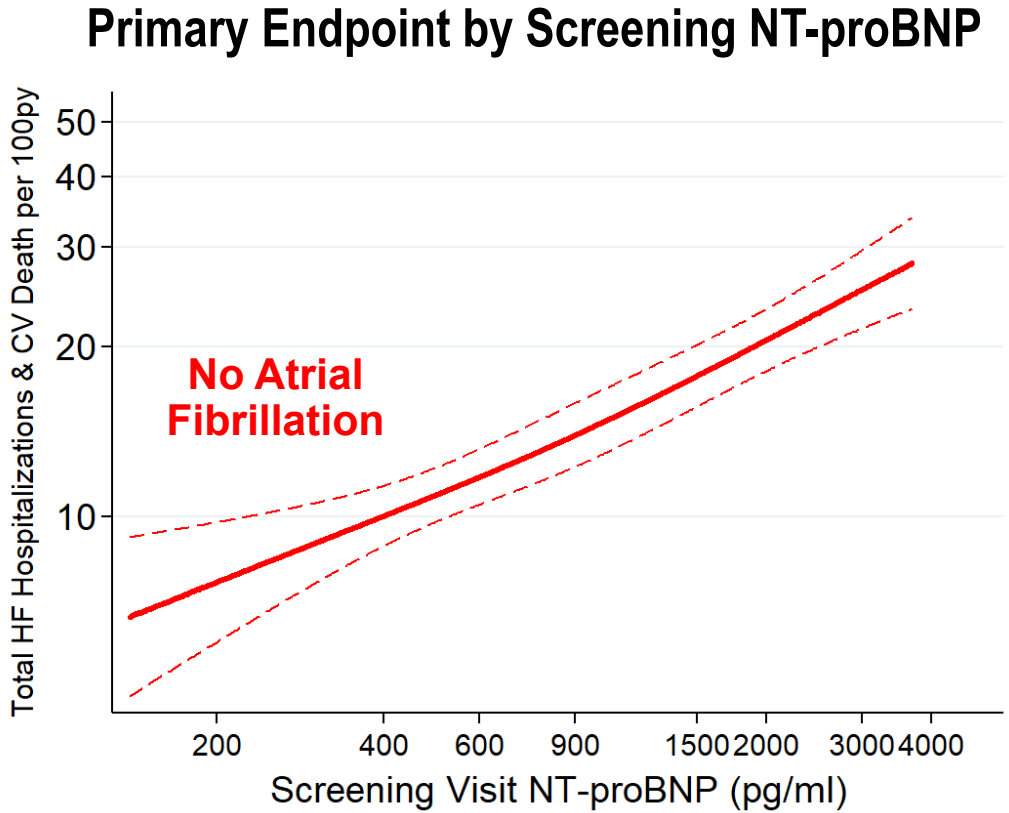
Baseline Characteristics in Each NT-proBNP Quartile

	Quartile 1 n=1190	Quartile 2 n=1189	Quartile 3 n=1189	Quartile 4 n=1190	P-value
NT-proBNP (pg/ml)	<464	465-911	912-1613	1617-31,522	
NYHA FC					<0.001
I	4%	3%	2%	2%	
II	79%	79%	78%	74%	
III	17%	18%	20%	23%	
IV	<1%	<1%	<1%	<1%	
BMI (kg/m^2)	31.1 ± 5.1	30.4 ± 4.9	31.1 ± 5.0	29.0 ± 4.8	<0.001
LVEF (%)	58.9 ± 7.9	57.8 ± 7.9	57.0 ± 7.6	56.3 ± 7.8	<0.001
eGFR ($ml/min/1.73m^2$)	67.3 ± 19.8	63.0 ± 18.7	61.6 ± 18.1	58.1 ± 18.4	<0.001

Baseline NT-proBNP strongly predicted total HF hosp & CV death



Atrial fibrillation modifies NT-proBNP risk prediction



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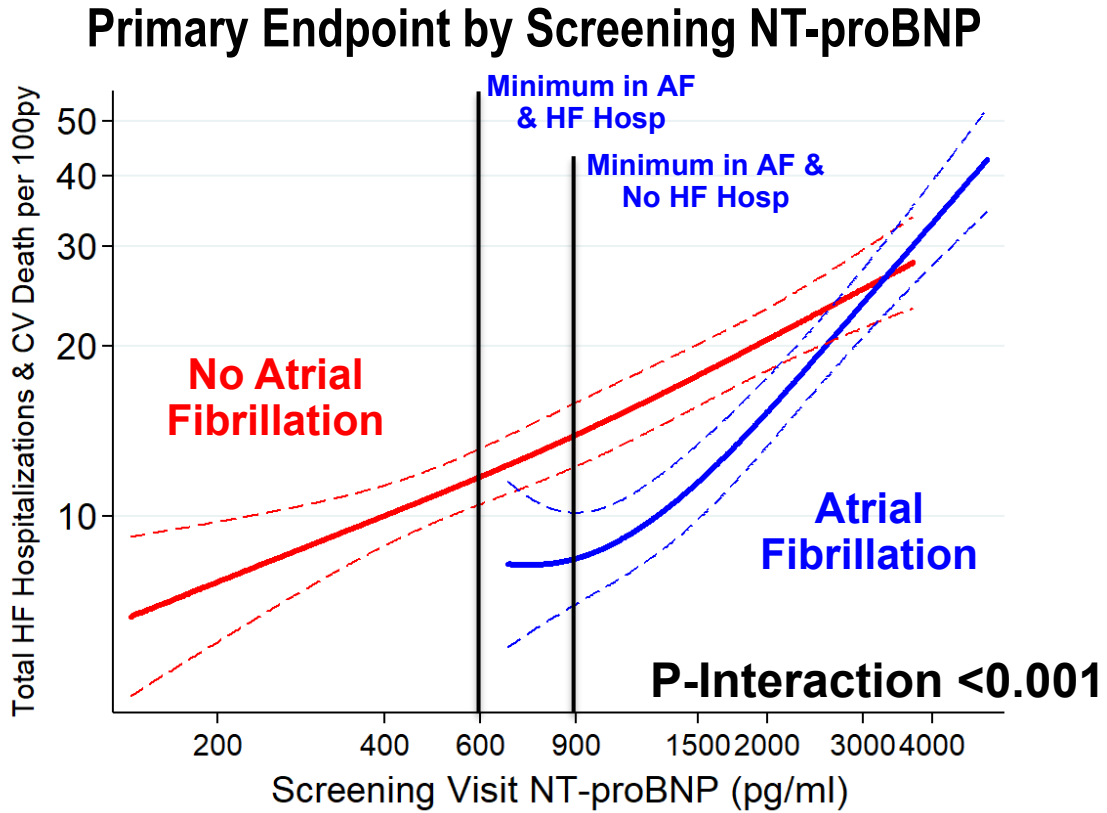
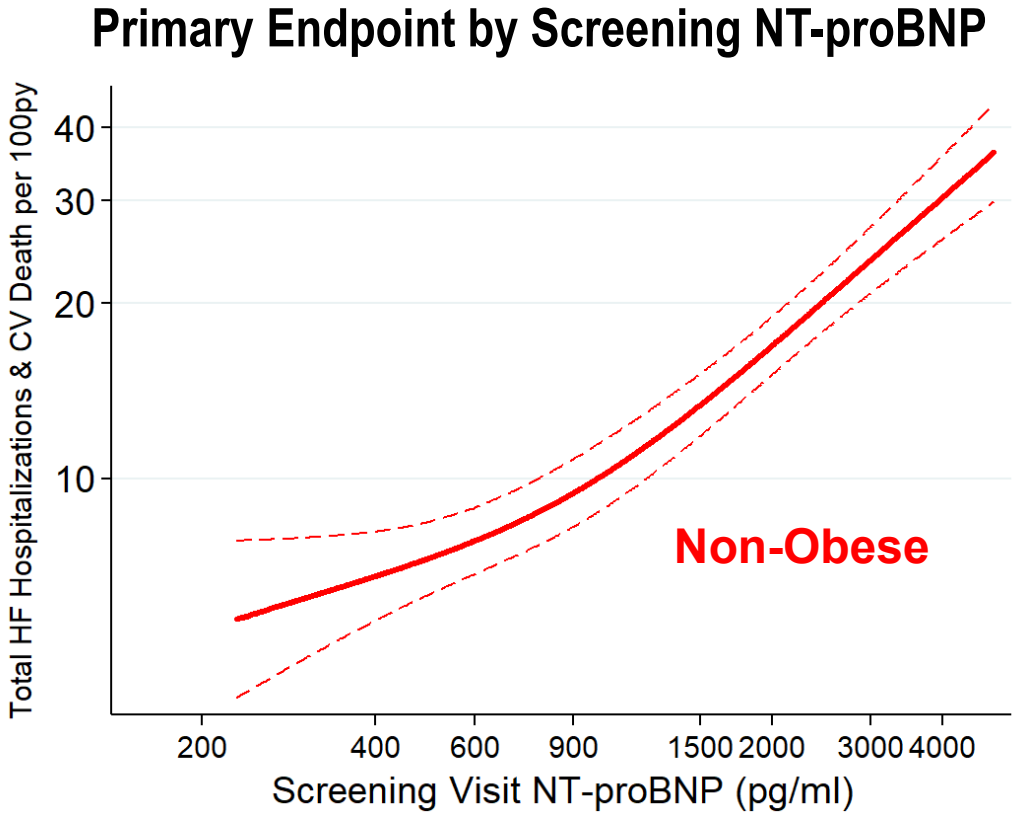


Obese patients with lower NT-proBNP retain moderate risk



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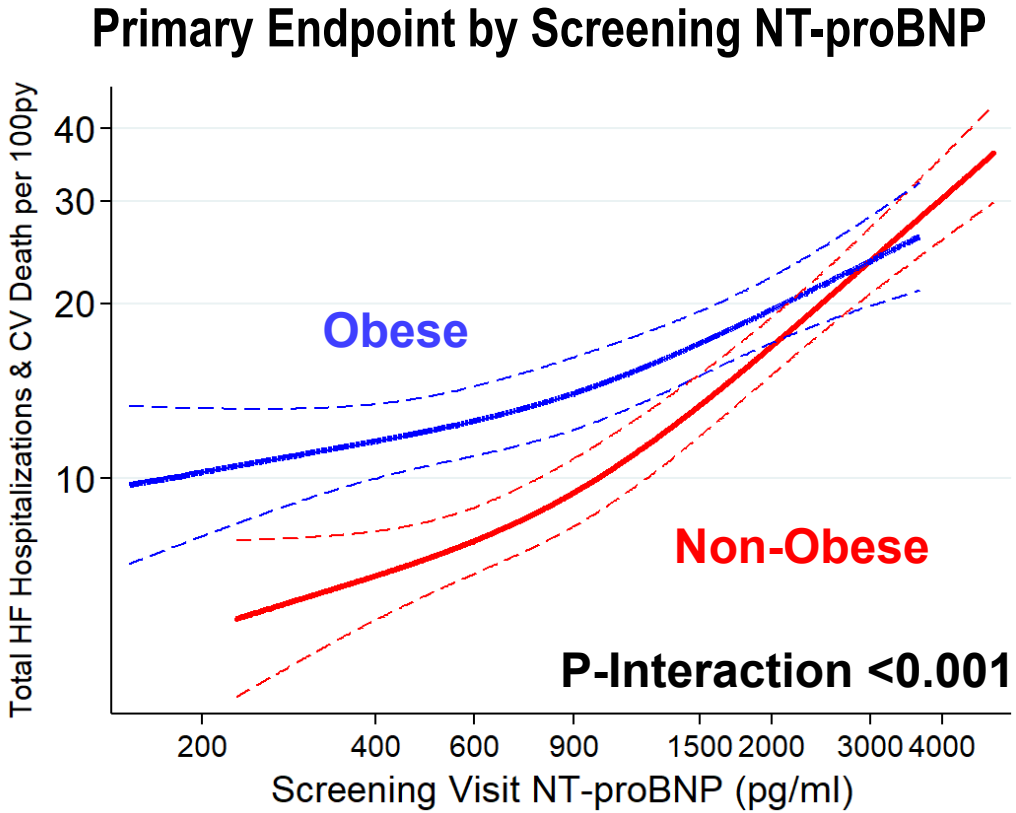
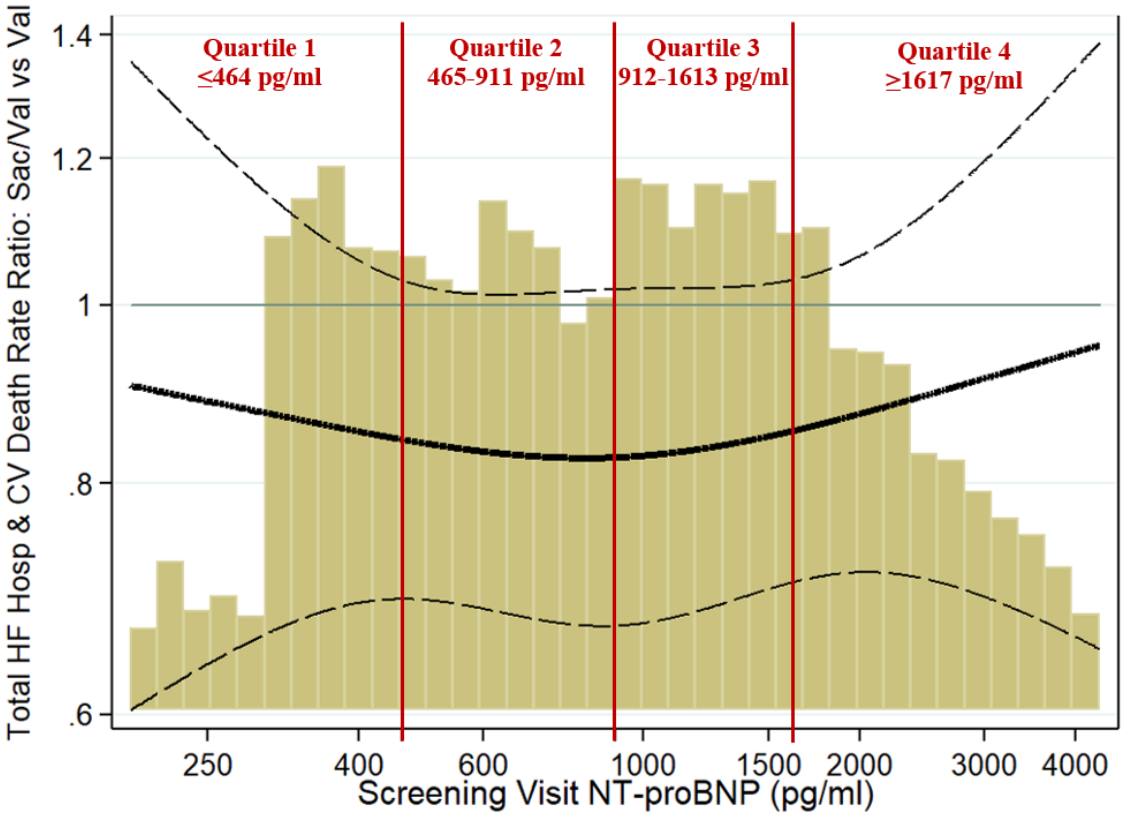
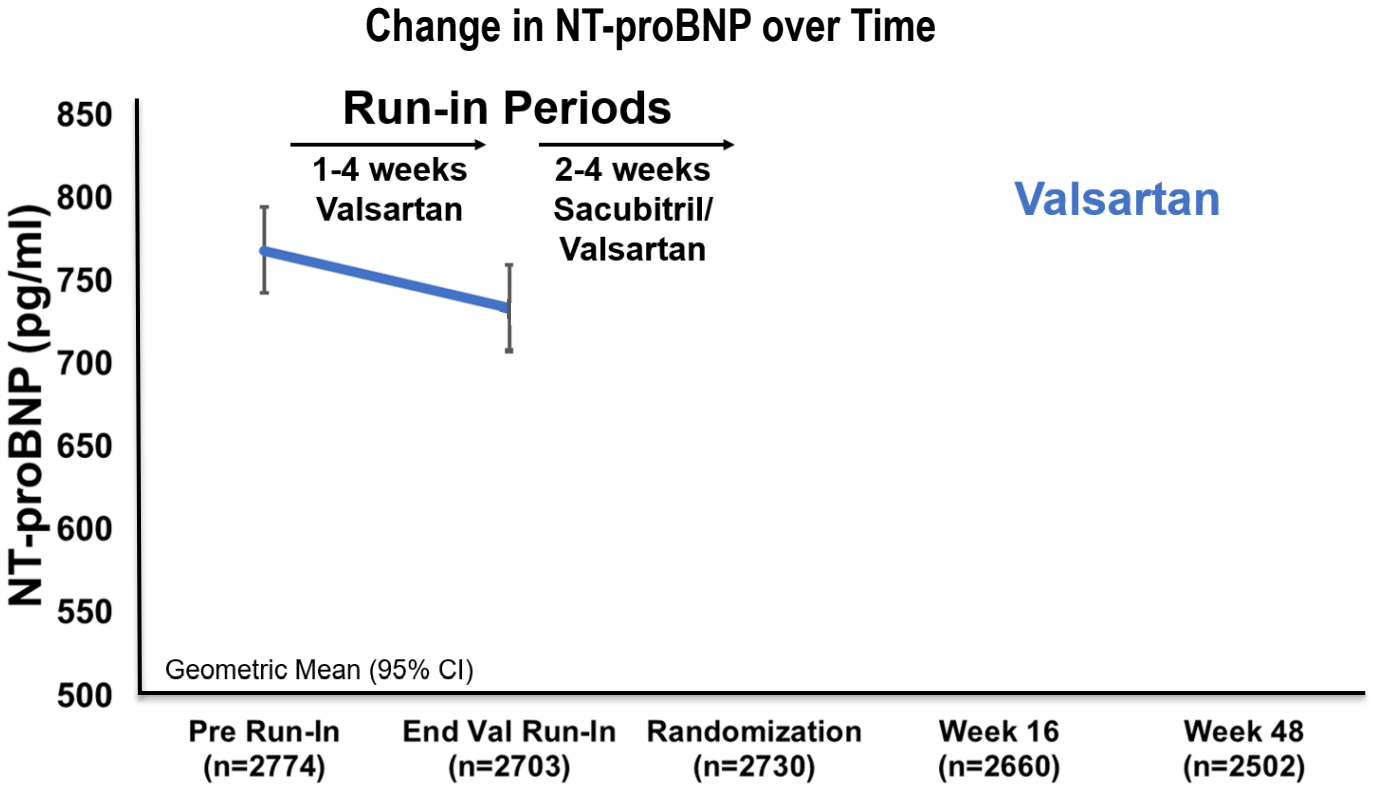


NT-proBNP Did Not Modify Sacubitril/Valsartan Treatment Effect



Sacubitril/valsartan reduced NT-proBNP by 19% (vs valsartan)



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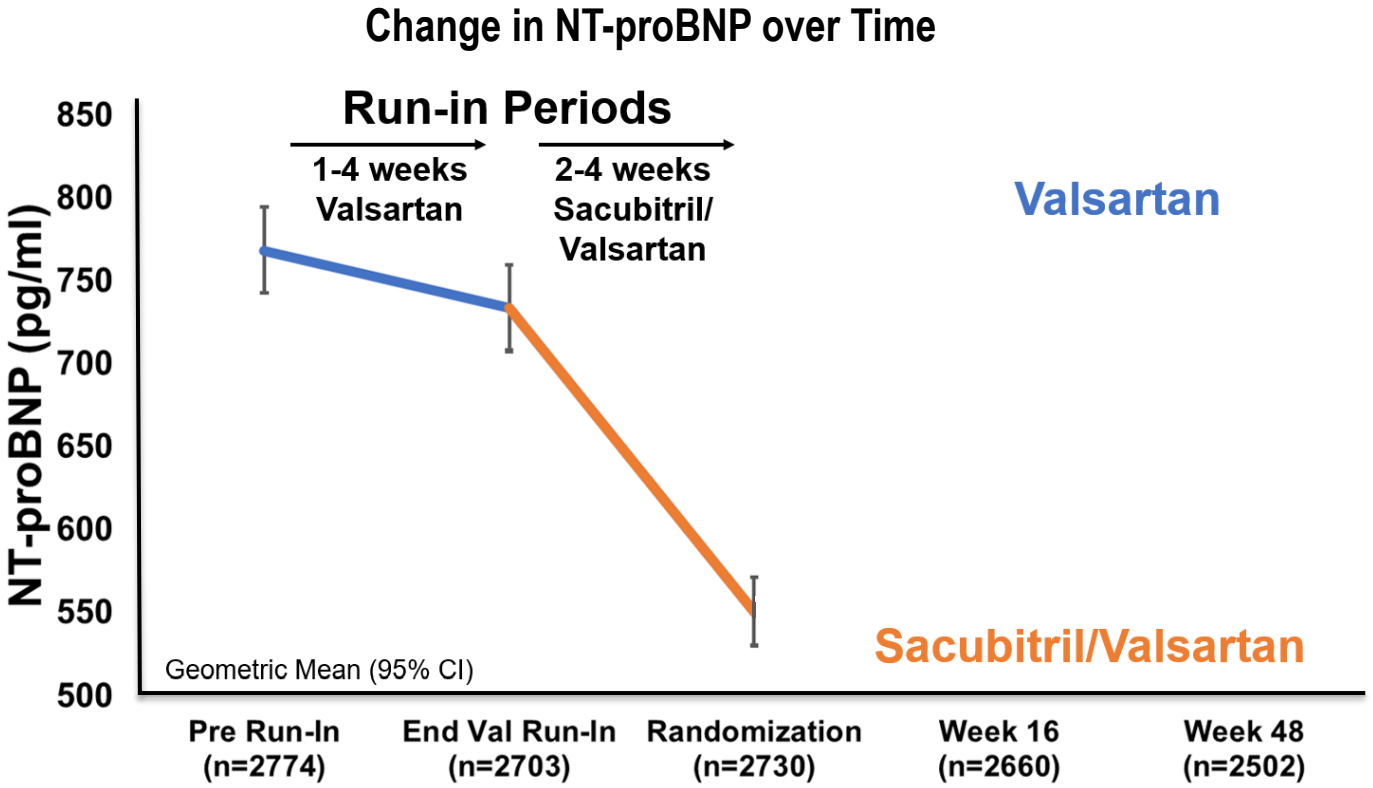

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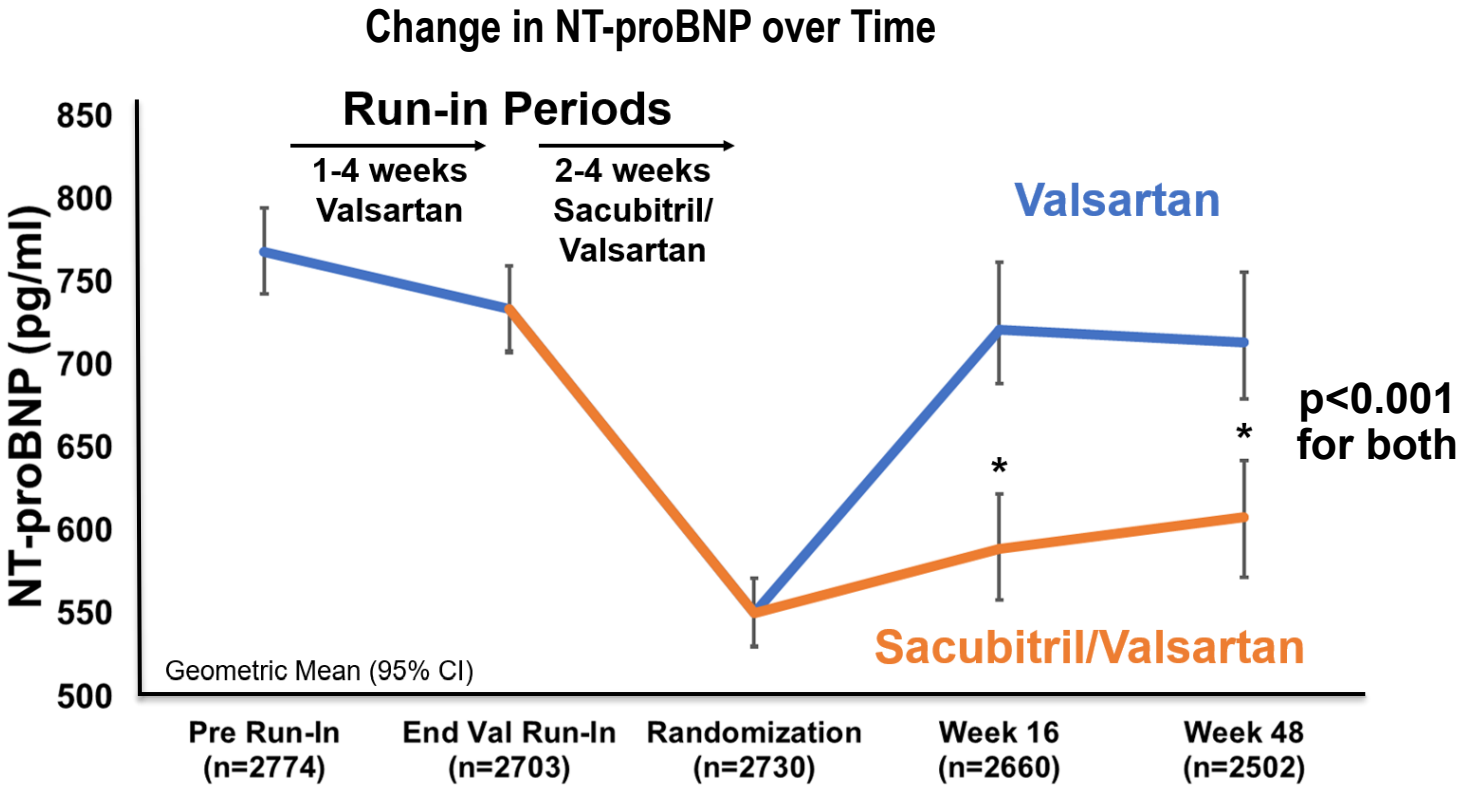
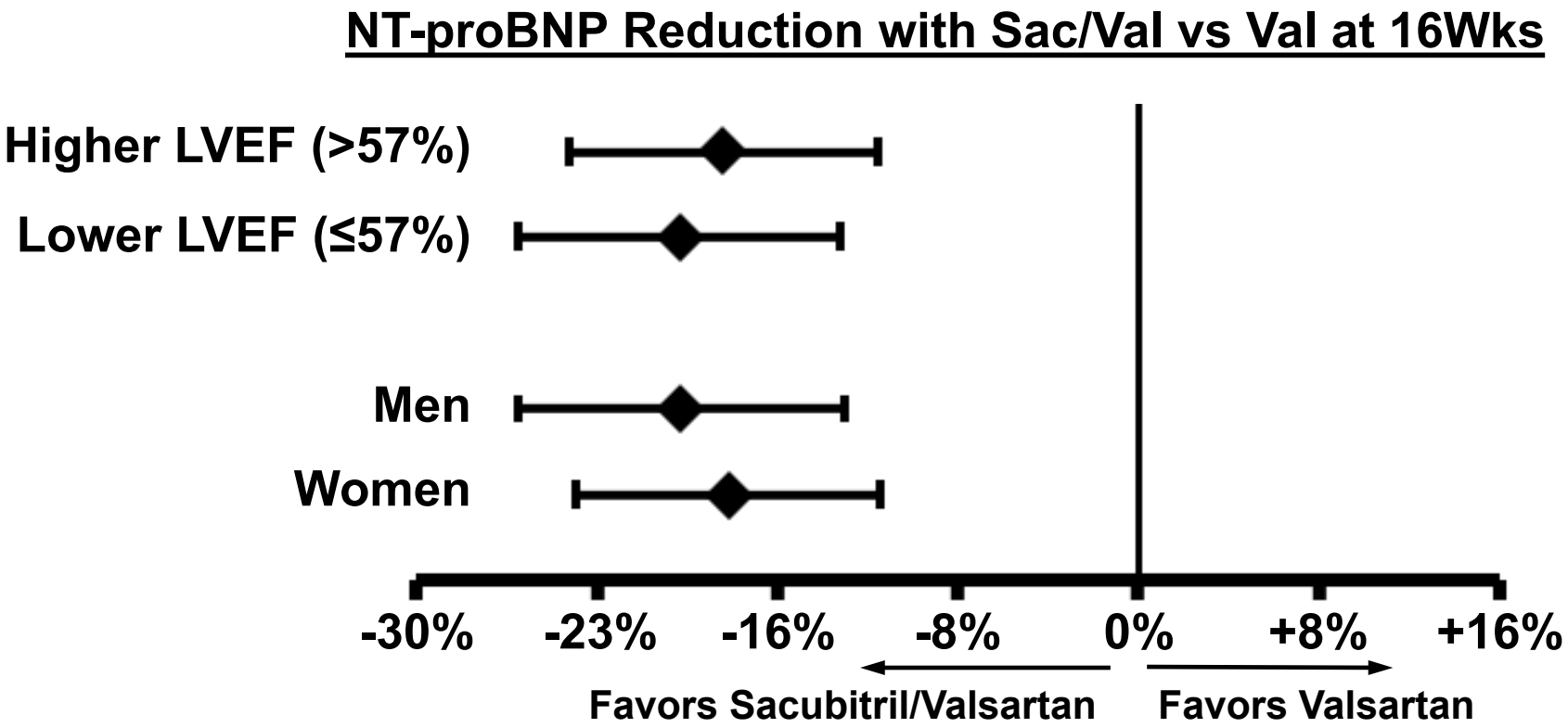
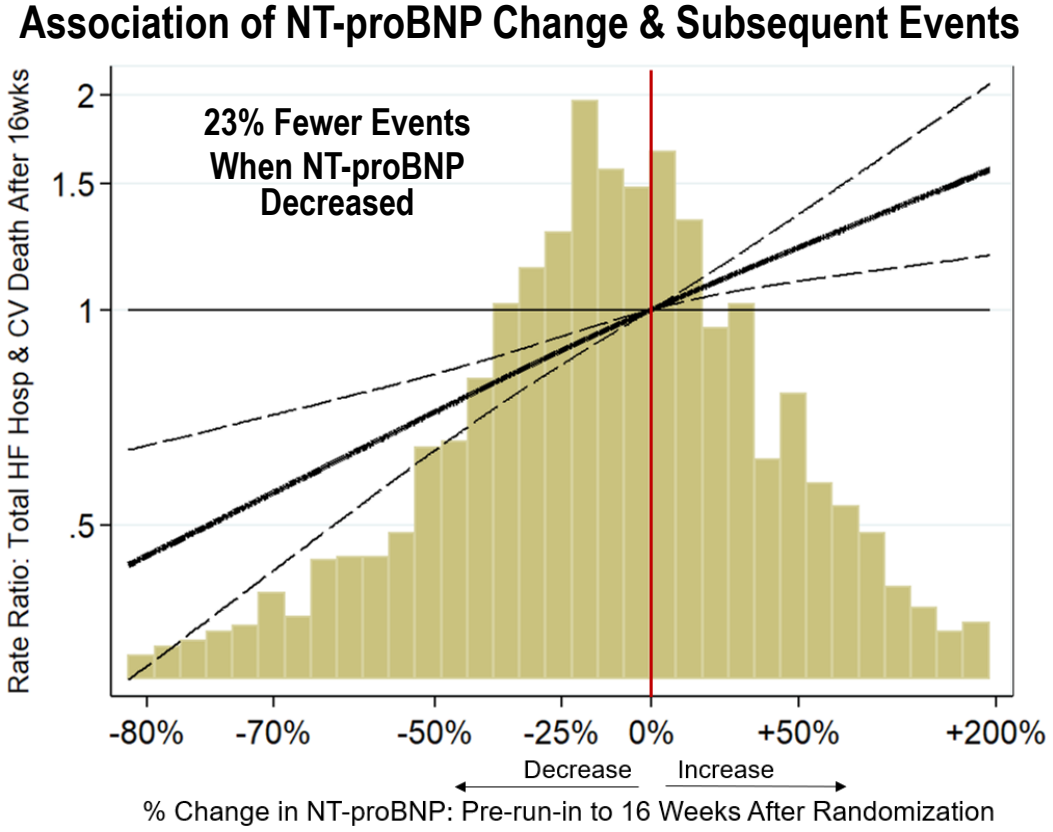


NT-proBNP Reduction Consistent in Key Subgroups



Decreases in NT-proBNP Associated with Lower Event Rate



Conclusions

NT-proBNP Risk Prediction

- NT-proBNP strongly predicted events in HFpEF
- Risk in atrial fibrilliation is lower for a given NT-proBNP
- Obese patients with low NT-proBNP retain moderate risk

Effects of Sacubitril/Valsartan

- Sacubitril/valsartan reduced NT-proBNP by 19% vs valsartan
- NT-proBNP reduction similar in men/women and lower/higher LVEF
- NT-proBNP did not identify patients who benefit more from sacubitril/valsartan

Simultaneous Publication in JACC: Heart Failure

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